Remarks

The Office Action mailed April 1, 2009, has been received and reviewed. Claims 1, 4, 9, and 11-13 having been amended, claims 5, 10 and 14-25 having been canceled, without prejudice, the pending claims are claims 1-4, 6-9, and 11-13. Of these, claims 3, 4, 7 and 12 have been withdrawn from consideration by the Examiner as drawn to a nonelected invention. Accordingly, claims 1, 2, 6, 8, 9, 11, and 13 currently under examination. Reconsideration and withdrawal of the rejections are respectfully requested.

The specification has been amended at page 6, lines 25-26, to recite "codon 309 to codon 489 of SEQ ID NO:1" in place of "nucleotide 309 to nucleotide 489 of SEQ ID NO:1". Support for this correction is found, for example, in the legend for Figs. 1B and 1C at page 4, lines 13 and 21, and in Figs. 1B and 1C. In the same paragraph, a typographical error (Gembank) has been corrected (Genbank).

Claims 1, 9, and 13 have been amended to recite "an Ebola glycoprotein containing a deletion of amino acids 309-489 of SEQ ID NO:1 in the *O*-glycosylation region." Support for this amendment can be found in the specification at, for example, page 4, lines 17-23; page 17, line 12; page 20, line 18; Figure 1; and in originally filed claim 10. Claim 4 has been amended to correct a dependency. Claims 11 and 12 have been amended to depend from claim 9, claim 10 having been canceled.

Rejection under 35 U.S.C. §112, second paragraph

The Examiner rejected claim 10 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, recitation of a deletion of "nucleotides" 309 to 489 in SEQ ID NO: 1 does not meet the description in the specification found at Para [0014].

Claim 10 has been canceled as a result of the amendment to claim 9, thereby rendering the rejection moot. Notwithstanding the claim cancellation however, Applicants submit that the

recitation of "nucleotides" 309 to 489 was an inadvertent error, and note that claim 9 correctly recites amino acids 309-489.

Reconsideration and withdrawal of the rejection of claim 10 under 35 U.S.C. §112, second paragraph, is accordingly requested.

Rejection under 35 U.S.C. §112, first paragraph

The Examiner rejected claims 1, 8, and 13 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. More specifically, the Examiner asserts that the specification has not explicitly defined "a modified *O*-glycosylation region" and therefore that a modified *O*-glycosylation region could be an amino acid sequence of any length that includes a glycosylation site. The Examiner concludes that the scope of the claims encompasses a genus of retroviruses pseudotyped with any glycoprotein that contains any modification. This rejection is respectfully traversed.

Applicants maintain that claims 1, 8 and 13 as originally filed meet the written description requirement. The term "*O*-glycosylation region" as recited in claims 1 and 13 as originally filed is described, for example, at page 6, lines 7-16 of the specification, and a modified *O*-glycosylation region is described, for example, at page 5, lines 6-11.

Nonetheless, in the interest of advancing prosecution, claims 1 and 13 are amended herewith to delete recitation of "a glycoprotein comprising a modified *O*-glycosylation region" and recite in its place "an Ebola glycoprotein containing a deletion of amino acids 309-489 of SEQ ID NO:1 in the *O*-glycosylation region." Claim 8 depends from claim 1 and thus includes all the features of amended claim 1. It is respectfully submitted the amendment overcomes the rejection and that claims 1, 8 and 13, as amended herewith, meet the written description set forth in 35 U.S.C. §112, first paragraph.

Reconsideration and withdrawal of the rejection of claims 1, 8 and 13, under 35 U.S.C. §112, first paragraph, is accordingly requested.

Rejection under 35 U.S.C. §102(b)

The Examiner rejected claims 1, 2, 5, 6, 9, and 11 under 35 U.S.C. §102(b) as being anticipated by Yang et al. (Nature Medicine, 6(8):886-889), as evidenced by Yang S. (Hum Gene Ther. 1999, Jan 1:10(1):123-132). This rejection is respectfully traversed.

Claim 5 has been canceled.

Claims 1 and 9 have been amended herewith to recite "an Ebola glycoprotein containing a deletion of amino acids 309-489 of SEQ ID NO:1 in the *O*-glycosylation region." The retrovirus taught in Yang et al., however, is pseudotyped with an Ebola glycoprotein containing a deletion of amino acids 315-505 (page 889, right-hand column). Yang et al. thus fail to teach the Ebola glycoprotein recited in claims 1 and 9, as amended herewith. Claims 2 and 6 depend from claim 1, and claim 11 has been amended to depend from claim 9; thus claims 2, 6 and 11 are also not anticipated by Yang et al.

Reconsideration and withdrawal of the rejection of claims 1, 2, 5, 6, 9, and 11, as amended herewith, under 35 U.S.C. §102(b) as being anticipated by the Yang et al. as evidenced by Yang is respectfully requested.

Rejection under 35 U.S.C. §102(b)

The Examiner rejected claims 1, 2, 5, 6, 9 and 11 as being anticipated by Simmons et al. (J. Virology, 76(5):2518-2528, 2002), in view of Wool-Lewis (J. Virology, 72(4):3155-3160, 1998), and Soneoka et al. (Nucleic Acid Res. 1995, Vol. 23(4):628-633). This rejection is respectfully traversed.

As noted above, claim 5 has been canceled.

Also as noted above, claims 1 and 9 have been amended herewith to recite a pseudotyped retrovirus comprising, *inter alia*, "an Ebola glycoprotein containing a deletion of amino acids 309-489 of SEQ ID NO:1 in the *O*-glycosylation region."

Simmons et al. teach serial deletions in the C-terminal mucin-like domain of Ebola glycoprotein; see Simmons et al., Fig. 3A. The modified Ebola glycoprotein designated

"mutΔ1234" contains the largest deletion, represented by amino acids 311-463, and lacks all of the predicted C-terminal *O*-linked glycosylation sites (Simmons et al., page 2520, second col., bridging to page 2521, first col.). Simmons et al. thus fail to teach "an Ebola glycoprotein containing a deletion of amino acids 309-489 of SEQ ID NO:1 in the *O*-glycosylation region" as recited in amended claims 1 and 9. Claims 2 and 6 depend from claim 1, and claim 11 has been amended to depend from claim 9; thus claims 2, 6 and 11 are also not anticipated by Simmons et al.

Reconsideration and withdrawal of the rejection of claims 1, 2, 5, 6, 9, and 11, as amended herewith, under 35 U.S.C. §102(a) as being anticipated by Simmons et al., in view of (i.e., as evidenced by) Wool-Lewis, and Soneoka et al. is respectfully requested.

Rejection under 35 U.S.C. §103(a)

The Examiner rejected claims 8 and 13 under 35 U.S.C. §103(a) as being unpatentable over either Yang et al. or Simmons et al., as applied to claims 1, 2, 5, 6, 9 and 11, and further in view of Wool-Lewis et al. This rejection is respectfully traversed.

As noted above, claim 1 (from which claim 8 depends) and claim 13 have been amended herewith to recite a retrovirus pseudotyped with "an Ebola glycoprotein containing a deletion of amino acids 309-489 of SEQ ID NO:1 in the *O*-glycosylation region." Claims 8 and 13 further recite that the pseudotyped retrovirus has a transduction efficiency into a target cell of at least 2-fold higher than a retrovirus pseudotyped with the wild-type glycoprotein.

Neither Yang et al. nor Simmons et al. teach a retrovirus pseudotyped with an Ebola glycoprotein containing a deletion of amino acids 309-489 in the *O*-glycosylation region as recited in claims 1 and 13, as amended herewith. Wool-Lewis et al. do not remedy this deficiency.

Yang et al., report a retrovirus pseudotyped with an Ebola glycoprotein containing a deletion of amino acids 315-505, as described in more detail above, and are silent with respect to transduction efficiency. Moreover, Yang et al. teach that "[t]he envelope glycoprotein mediated

cytotoxic effects" (page 888, left-hand column) thus increases in transduction efficiency would be considered detrimental.

Simmons et al. describe a retrovirus pseudotyped with an Ebola glycoprotein containing a deletion of amino acids 311-463 (mutΔ1234), as mentioned above. With respect to transduction efficiency, Simmons et al. teach that coexpression of mutΔ1234 with plasmids encoding MLV Gag/Pol and LacZ produced infectious MLV pseudotype particles with titers "*equivalent* to those of wild-type EboZ GP" (emphasis added; page 2521, left-hand column).

Applicants respectfully submit that amendment of claim 1 (from which claim 8 depends) and claim 13 to recite a retrovirus pseudotyped with "an Ebola glycoprotein containing a deletion of amino acids 309-489 of SEQ ID NO:1 in the *O*-glycosylation region" overcomes the rejection under 35 U.S.C. §103(a). The deleted region specified in the instant claims, as amended, is not merely an obvious variant of the deleted regions described in Yang et al. or Simmons et al. Moreover, the pseudotyped retroviruses taught in Yang et al. and Simmons et al. are not shown to have higher transduction efficiencies compared to retroviruses pseudotyped with wild-type Ebola GP, as exhibited by the pseudotyped retroviruses as presently claimed (e.g., claims 8 and 13). Applicants' deletion of amino acids 309-489 from Ebola glycoprotein unexpectedly resulted in a modified glycoprotein that, when used for pseudotyping, significantly increases transduction efficiencies. See, e.g., the specification at page 19, lines 11-12, wherein the Applicants state that "[r]emarkably, processing and viral incorporation of the Δ309-489 GP was greatly enhanced as shown in Figure 2" and page 19, lines 27-28, "[t]he effect of deleting the *O*-glycosylation region of GP1 (Δ309-489) on expression and transduction were striking."

It is therefore submitted that claims 8 and 13 are not obvious over Yang et al. or Simmons et al., in view of Wool-Lewis et al. Reconsideration and withdrawal of the rejection of claims 8 and 13 under 35 U.S.C. §103(a) as being unpatentable over either Yang et al. or Simmons et al., and further in view of Wool-Lewis et al., is accordingly requested.

Request for Rejoinder

Species elections were required by the Examiner in the Office Action dated October 31, 2007. It is understood that (a) the requirement for species election will be withdrawn upon the finding of an allowable genus; and (b) any species withdrawn from consideration will be transferred to the elected subject matter unless it is found patentably distinct from the elected or allowed claims.

Applicants respectfully submit that claims 1, 2, 6, 8, 9, 11 and 13, as amended herewith, are in condition for allowance.

In view thereof, Applicants kindly request withdrawal of the species elections and rejoinder of claims 3, 4, 7, and 12, which currently stand withdrawn. Claims 3, 4 and 7 depend from claim 1, which, as amended, which remains generic. Claim 12, as amended, depends from claim 9, which also remains generic. With respect to the genus of retroviral core and control elements, Applicant wish to draw the Examiner's attention to Example III in the specification, beginning at page 21, which describes a retrovirus with a FIV core and control elements (see, e.g., claims 3, 4 and 12), pseudotyped with an Ebola glycoprotein containing a deletion of amino acids 309-489 in the *O*-glycosylation region as recited in claim 1 (from which claims 3 and 4 depend) and claim 9 (from which claim 12 depends).

Summary

It is respectfully submitted that the pending claims 1-4, 6-9 and 11-13 are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to contact Applicants' Representatives at the telephone number listed below if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted
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CERTIFICATE UNDER 37 CFR §1.8:
The undersigned hereby certifies that this paper is being transmitted via the U.S. Patent and Trademark Office electronic filing system in accordance with 37 CFR §1.6(a)(4) to the Patent and Trademark Office addressed to the Commissioner for Patents, **Mail Stop Amendment**, P.O. Box 1450, Alexandria, VA 22313-1450, on this 22nd day of July 2009.

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